specified formula.

37 CFR 1.475(d) says that if "multiple products" are claimed, the first such invention will be considered the main invention. In effect, that means that if the USPTO is acting as ISA or IPEA, and finds that those multiple products lack unity under PCT rule 13.2, the first product claimed will be the one that is searched.

2.1. Unity is normally analyzed in the first instance only with respect to the independent claims in the PCT sense, i.e., a claim of a particular category that does not reference another claim of the same category. See PCT Administrative Instructions, Annex B, paragraph (c). The only such product claim is claim 1. Paragraph (c)(i) says "no problem arises in the case of a genus/species situation where the genus claim avoids the prior art".

The special technical feature linking the claims is the combination of structural elements, i.e., the amino acid sequence of the formula L1-A-L2-B-L3-C-L4-D-L5 and the linker X[(A)nCOOH][(B)mCOOH].

The examiner has failed to cite prior art against claim 1 and thereby establish a posteriori lack of unity. Hence claim 1, being generic in form, prima facie unifies all of the compounds it covers.

2.2. We are aware that PCT Administrative Instructions paragraph (f) has special rules for Markush claims. But claim 1 is not a Markush claim, although some elements are defined by Markush groups. Claim 11 is, but it is a dependent claim within the meaning of paragraph (c). Paragraph (f) comes into play only if the independent claim is a Markush claim (not true here), or if the independent claim is held to lack unity a posteriori and hence it is necessary to separately evaluate the unity of the dependent Markush claim.

For the sake of completeness, we will pretend that the examiner had in fact established a posteriori lack of unity as to claim 1, and hence it was necessary to analyze claim 11 in

accordance with paragraph (f).

2.3. The first issue is whether "all alternatives have a common property or activity", see (i)(A).

Claim 1 has been amended to require that the component peptide and the compound be capable of binding to fibroblast growth factor receptor. Since claim 11 is dependent on 1, it includes this limitation.

2.4. Secondly, it is necessary that "a common structure is present, i.e., a significant structural element is shared by all of the alternatives". The common structural elements defined by claim 1 are first that the peptide comprises (1) a hydrophobic AA (Leu/Ile/Val/Phe, Trp/Tyr), (2) an amino acid which is Arg/Lys/His/Asn/Gln, (3) Asp/Glu/Asn/Gln, (4) Gly/Ala[1], and second that the compound comprises the defined linker.

However, there are the further structural elements defined by the limitation of amended claim 11 to particular SID's. These have a minimum of 3 aa positions that are identical to SID 1. We enclose, as Exhibit 1, an alignment of SID1 with SID2-8, 11-73, 97-99, and 114-145. Claim 11 has been amended on even date herewith to strike the other sequences (as well as additional sequences inconsistent with base claim 1).

The elected sequences SID1 and 2 show a common motif, see the bolded (identical) and underlined (positive match) amino acids:

SEQ ID NO:1 **EV**<u>**Y**</u>**VVAEN**QQ**GK**SKA
SEQ ID NO:2 NI**EV**<u>**W**</u>**VEAEN**AL**GK**KV

By sequence alignment, it may be shown that at least 82 of the originally claimed peptide sequences share a structural relationship (Exhibit 1) with SID1. Of these, 69 sequences satisfy the motif of claim I, and can thus be included in a group with a common motif. Only those 69 are now recited in claim 11.

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[1] See definitions at P18, L17-21.

From the sequence listing, the origins of the peptide sequences are evident; they are not all derived from NCAM. However, they are all derived from a protein with an FGFR binding motif, and comprise at least part of said FGFR binding motif. There is thus an expectation of functionality.

The choice of the linker that connects the two peptide sequences in the dimer compound cited in claim 1 may also influence the activity of the compound, see WO00/18791. Thus, the linker contributes to the functional relationship.

2.5. We note that claims 7-10 do not read on SID 1 or 2.

3. The examiner also asserts that "unrelated methods" are claimed (OA page 3, lines 6-7). This is not explained until the last paragraph of page 4:

> The different conditions, diseases and disorders comprise a diverse spectrum of medical disorders that are unique in terms of their diagnosis, etiology, pathology, and affected populations and therefore the different species do not relate to a general inventive concept under PCT Rule 13.1.

We are therefore required to elect a disease or condition from claims 22-32. It is not clear if this requirement applies, as we elected group I but claims 22-32 are in II. However, for sake of completeness we elect Alzheimer's Disease with traverse.

4. All diseases in our opinion should be grouped together because of a common mechanism allowing them to be treated by the same peptide sequences, capable of modulating FGFR signalling.

FGFR signalling is involved in a number of cellular processes, which are all related to cellular disorders and accompanying disease states when dysregulated.

Overall, FGFR modulation has various effects that may revert some disease conditions. Activation of the FGF receptor promotes cell survival and cell proliferation, induces angiogenesis and induces differentiation, among other effects. These effects of

FGFR modulation may be advantageously exploited in an array of disease conditions in which promotion of cell survival and cell proliferation and the induction of angiogenesis and differentiation is desirable for treating said conditions (see the sections in the application as filed re. 'Medicament' on page 58 ff and 'Treatment' on page 67 ff).

Promoting cell survival, differentiation and angiogenesis is desirable e.g. in an array of neuronal diseases, muscle diseases, diabetes mellitus, wound healing and ischemic conditions. As these effects are achievable by use of the dimer compounds of the present invention, via a modulation of the FGFR, it would be unduly limiting to select only one condition to be treated by the compound of the present invention.

While most conditions will benefit from an activation of the FGFR, causing differentiation, angiogenesis, proliferation and survival, there are instances where the FGFR modulation according to the present invention may promote cell survival of one cell type, and promote cell death of another cell type (page 58 lines 34). Thus it may be cell type specific.

Respectfully submitted,

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Enclosure
-Exhibit 1: Sequence Alignment (2 pp.)

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